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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,909	BRON, DENIS	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) 4-28 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3 is/are rejected.

7)☒ Claim(s) 4-28 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-28 are pending and under examination.

Claim Objections

2. Claims 4-28 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot serve as a basis for any other multiple dependent claims, either directly or indirectly. In the instant case, the multiple dependent claims 4-28 directly or indirectly depend from the multiple dependent claim 2. See MPEP § 608.01(n). Additionally, claims 26-28 are in improper form because they do not refer to the other claims in the alternative only.

Accordingly, the claims 4-28 have been withdrawn from examination and not been further treated on the merits.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to the foreign application EPO 02014991.0. However, the disclosure of the foreign application EPO 02014991.0, fails to provide adequate support or enablement for one or more claims of this application.

The instant claims 1-28 disclose a delivery system comprising the NCAM Ig loop domains I, II, and III, wherein the delivery system further comprises an integrase (claims 26 and 27). The Application EPO 02014991.0 does not provide support for the use of

the NCAM Ig loop domains I, II, and III or for the use of an integrase. Therefore, the priority date for these embodiments is considered to be the filing date of the PCT/CH03/00453, i.e., 07/08/2003.

Should Applicant disagree, Applicant is encouraged to point out with particularity by page and line number where such support might exist in each intervening document. In order to properly claim priority, the support for each of the claim limitations must exist in each of the intervening documents.

Information Disclosure Statement

4. The information disclosure statement filed 01/10/2005 fails to comply with 37 CFR 1.98(a)(2), because an English translation of the foreign document DE 100 56 136 has not been provided. It has been placed in the application file, but the foreign document DE 100 56 136 has not been considered.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poulsen et al. (PGPUB 2005/0037445), in view of each Maurer et al. (Expert Opin Biol

Ther, 2001, 1: 923-947), Ranheim et al. (Proc Natl Acad Sci USA, 1996, 93: 4071-4075), and Schreier et al. (J Biol Chem, 1994, 269: 9090-9098).

Poulsen et al. teach a delivery system for bioactive agents (i.e., pharmaceutical agents), wherein the system comprises a bioactive agent such as nucleic acids encoding therapeutic proteins and a binding partner capable of associating with a cell surface receptor (i.e., a targeting moiety); when the bioactive agent is a nucleic acid, the delivery system further comprises polycations, wherein the polycations form particles comprising the nucleic acid in their internal compartment and wherein the polycations form a bridge between the nucleic acid and the targeting moiety, i.e., the targeting moiety is on the particle surface (claim 1) (p. 33, paragraphs 0390-0394, p. 34, paragraphs 0412-0418, p. 39, paragraphs 0563-0565, 0570, and 0571). Poulsen et al. teach that the targeting moiety can be NCAM (claim 1) or NCAM IgI+II or IgIII domains (claims 1 and 2) (p. 30, paragraphs 0346, 0355, and 0357, p. 31, paragraphs 0358-0360).

Although Poulsen et al. teach that liposomes in general could be used to deliver nucleic acids (p. 1, paragraph 0004), they do no specifically teach liposomes as the bridge between the nucleic acid and the targeting moiety (claim 1). Maurer et al. teach liposomes as the leading delivery system for the *in vivo* administration of nucleic acids (Abstract, p. 941, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Poulsen et al. by substituting the polycations with liposomes, with a reasonable expectation of success. The motivation to do so is provided by Maurer et al., who teach liposomes as the leading delivery

system for systemic administration of nucleic acids, wherein liposomes are versatile carriers because they can be easily modified by insertion of diverse molecules, such as targeting ligands, to suit any particular application (p. 923, column 1, p. 926, paragraph bridging p. 927, p. 927, column 1, last paragraph). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that liposomes can be successfully used to target nucleic acids to the cell/tissue of interest. Poulsen et al. taken with Maurer et al. do not teach linking the NCAM via a hydrophobic anchor molecule (claim 3). However, this is not innovative over the prior art. For example, Schreier et al. teach targeting liposomes to specific cells by inserting ligands into liposomes via a glycosylphoshaphatidylinositol (GPI) anchor (i.e., a hydrophobic anchor molecule) (Abstract, p. 9092, columns 1 and 2, p. 9093, columns 1 and 2, p. 9097, column 1, paragraph bridging column 2, 9098, column 1, last paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the delivery system of Poulsen et al. and Maurer et al. by inserting the NCAM ligand via a GPI anchor, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because Schreier et al. teach their method as simple and convenient (p. 9090, column 2, first full paragraph). One of skill in the art would have been expected to have a reasonable expectation of success because the art teaches the successful use of GPI anchors to incorporatate proteins into liposomes.

With respect to the limitation recited in claim 2, although Poulsen et al. teach using an NCAM fragment comprising the IgI and IgII domains or an NCAM fragment

comprising IgIII domain as targeting ligands, they do not teach using a fragment comprising all IgI, IgII, and IgIII domains of NCAM. However, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the delivery system of Poulsen et al. by adding the IgIII domain to their IgI+IgII fragment for increased binding to NCAM on the target cell surface, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the art teaches that, beside the IgI and IgII domains, the IgIII domain also contributes to the binding to NCAM (see Poulsen et al., p. 31, paragraphs 0358-0360; Ranheim et al., p. 4074, column 2, and Fig. 6). One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that all three Ig NCAM domains are involved in homophilic binding to the NCAM molecule expressed on the surface of the target cell.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

7. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy (U.S. Patent No. 6,635,476), in view of Poulsen et al. and Ranheim et al.

Murphy teaches a system for the delivery of a therapeutic agent, the system comprising liposomes having on their surface a targeting ligands, which target cell surface receptors such as NCAM, and a therapeutic agent in their internal space (claim 1) (Abstract, column 3, lines 5, 6, and 59-63, column 5, lines 24-27, column 9, lines 45-50, column 13, lines 25-46). Although Murphy teaches that any ligand which binds to

the cell surface receptor could be used as a targeting ligand (column 13, lines 50-61), he does not specifically teach NCAM or an NCAM fragment comprising the first three Ig domain as targeting ligands (claims 1 and 2). Poulsen et al. teach using NCAM, an NCAM fragment comprising the IgI and IgII domains, or an NCAM fragment comprising IgIII domain as targeting ligands capable of homophilic binding to another NCAM molecule on the surface of a target cell (p. 3, paragraph 0036, p. 4, paragraphs 0048-0051, p. 28, paragraphs 0288 and 0290, p. 29, paragraphs 0355, p. 31, paragraphs 0358-0360). It would have been obvious to one of skill in the art, at the time the invention was made, to modify Murphy's delivery system by using one of the targeting ligands taught by Poulsen et al., with a reasonable expectation of success. One of skill in the art would have been motivated to do so and would have been expected to have a reasonable expectation of success in doing so because Murhpy teaches that any ligand that binds NCAM can be used with their system. With respect to the limitation recited in claim 2, it would have been obvious to one of skill in the art, at the time the invention was made to combine the IgIII and IgI+IgII fragments of Poulsen et al. to obtain an IgI+IgII+IgIII fragment, for increased binding to NCAM on the target cell surface, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the art teaches that, besides the beside IgI and IgII domains, the IgIII domain, also contributes to the binding to NCAM (see Poulsen et al., p. 31, paragraphs 0358-0360; Ranheim et al., p. 4074, column 2, and Fig. 6). One of skill in the art would have been expected to have a reasonable expectation of success in doing such

because the art teaches that all three Ig NCAM domains are involved in homophilic binding to the NCAM molecule expressed on the surface of the target cell.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

Art Unit 1633